

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

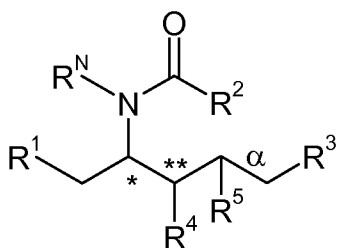
Claims 1-91. (Canceled)

92. (Currently Amended) A pharmaceutical formulation comprising:

(i) a drug; and

(ii) a short-chain sphingolipid selected from compounds of the following

formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted

amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group;

R² is independently C₃₋₉alkyl,

and is independently unsubstituted or substituted;

R^3 is independently C_{7-19} alkyl,

and is independently unsubstituted or substituted;

R^4 is independently -H, -OH, or -O- C_{1-4} alkyl;

R^N is independently -H or C_{1-4} alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an
S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an
S-configuration;

and pharmaceutically acceptable salts, ~~solvates, esters, and ethers~~
thereof.

93. (Previously Presented) A pharmaceutical formulation according to claim 92,
wherein said drug is an amphiphilic drug.

94. (Previously Presented) A pharmaceutical formulation according to claim 92,
wherein said drug is an anthracycline.

95. (Previously Presented) A pharmaceutical formulation according to claim 92,
wherein said drug is selected from: doxorubicin, idarubicin, epirubicin, aclarubicin,
mitrozantrone, and daunorubicin, and salts thereof.

96. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is doxorubicin or doxorubicin hydrochloride.

97. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is an alkaloid.

98. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: topotecan and camptothecin.

99. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ linear.

100. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ linear; and has from 0 to 3 carbon-carbon double bonds.

101. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ unsubstituted or substituted with from 1 to 3 substituents selected from C_{1-4} alkyl, -OH, C_{1-4} alkoxy, -C(=O)OH, and -C(=O)O- C_{1-4} alkyl.

102. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ $-(CH_2)_nCH_3$, wherein n is an integer from 4 to 8.

103. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ $-(CH_2)_nCH_3$, wherein n is an integer from 6 to 8.

104. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^2 is ~~independently~~ $-(CH_2)_6CH_3$.

105. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is ~~independently~~ a double bond and R^5 is -H.

106. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is ~~independently~~ a single bond; and R⁵ is -H.

107. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is ~~independently~~ a single bond; and R⁵ is -OH.

108. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R³ is ~~independently~~ linear.

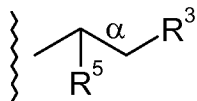
109. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R³ is ~~independently~~ linear; and has from 0 to 3 carbon-carbon double bonds.

110. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R³ is ~~independently~~ unsubstituted or substituted with from 1 to 3 substituents selected from C₁₋₄alkyl, -OH, C₁₋₄alkoxy.

111. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R³ is ~~independently~~ -(CH₂)_nCH₃, wherein n is an integer from 8 to 16.

112. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R³ is ~~independently~~ -(CH₂)₁₂CH₃.

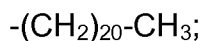
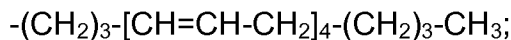
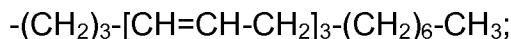
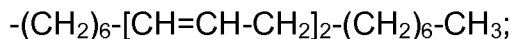
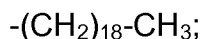
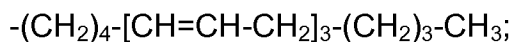
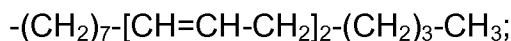
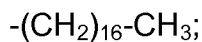
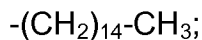
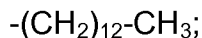
113. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein the moiety:



is selected from the following:

-(CH₂)₈-CH₃;

-(CH₂)₁₀-CH₃;



analog of the foregoing wherein the left-most $-(\text{CH}_2)_2-$ is replaced with $-\text{CH}=\text{CH}-$; and

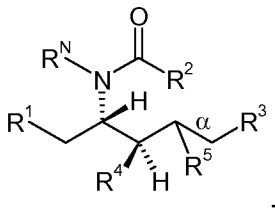
analog of the foregoing wherein the left-most $-(\text{CH}_2)-$ is replaced with $-\text{CH}(\text{OH})-$.

114. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^4 is independently $-\text{H}$, $-\text{OH}$, $-\text{OMe}$, $-\text{OEt}$, $-\text{O}(\text{iPr})$, $-\text{O}(\text{nPr})$, $-\text{O}(\text{nBu})$, $-\text{O}(\text{iBu})$, $-\text{O}(\text{sBu})$, or $-\text{O}(\text{tBu})$.

115. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R⁴ is ~~independently~~ -OH.

116. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^N is ~~independently~~ -H, -Me, or -Et.

117. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein the carbon atoms marked (*) and (**) have a configuration as shown in the following formula:



118. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~ an O-linked saccharide group.

119. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~ an O-linked mono-, di-, or tri-saccharide group.

120. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is comprises ~~formed from~~ a group or groups selected from:

arabinose, lyxose, ribose, [[or]] xylose[[:]],

allose, altrose, glucose, mannose, gulose, idose, galactose,

[[or]]and talose;

and derivatives thereof.

121. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~ an O-linked mono-, di-, or tri-saccharide group comprising a group or groups selected derived from:

arabinose, lyxose, ribose, [[or]]xylose[[:]],

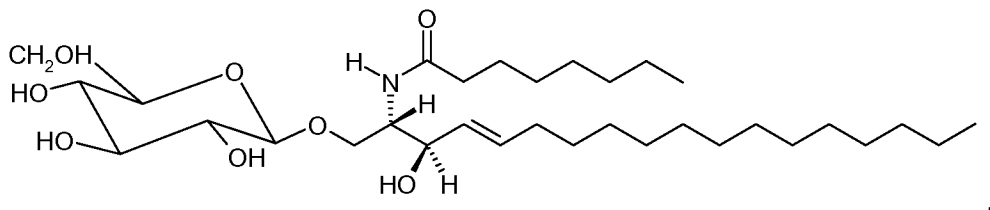
allose, altrose, glucose, mannose, gulose, idose, galactose, [[or]]
talose[[:]],

sucrose, maltose, lactose, cellobiose, [[or]]galabiose[[:]],

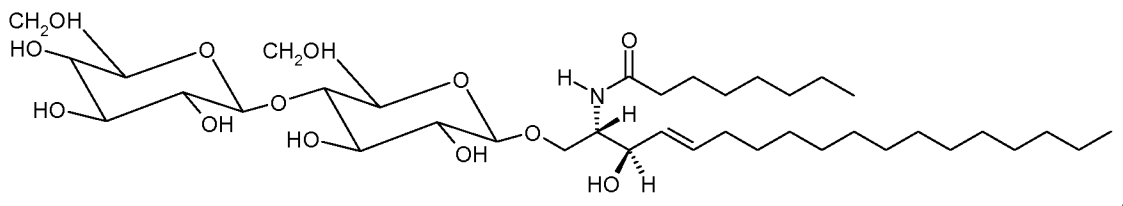
globotriaose, isoglobotriaose, mucotriaose, lactotriaose,
neolactotriaose gangliotriaose, galatρίαose, mollutriaose, [[or]]and antrotriaose;
~~or a derivative~~ and derivatives thereof.

122. (Currently Amended) A pharmaceutical formulation according to claim 120, wherein said saccharide group derivatives are selected from deoxy, di-deoxy, di-deoxy-di-dehydro, methoxy (-OMe), acetoxy (-OC(=O)Me), carboxylic acid (-C(=O)OH), sulfuric acid (-OSO₃H), amino-deoxy ([[e.g.,]] -NH₂), N-acetyl-amino-deoxy ([[e.g.,]] -NHC(=O)Me), or N-sulfo-amino-deoxy ([[e.g.,]] -NHS(O)₂OH) derivatives.

123. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula (C₈-GlcCer):



124. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula:



125. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~ an O-linked polyhydric alcohol group.

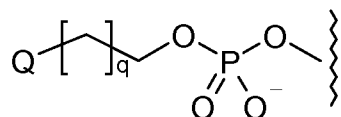
126. (Currently Amended) A pharmaceutical formulation according to claim 125, wherein R¹ ~~is formed from groups~~ comprises a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

127. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group.

128. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R¹ is ~~independently~~:



wherein:

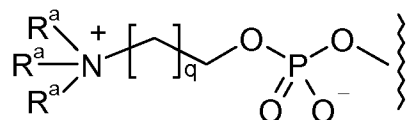
q is ~~independently~~ an integer from 0 to 5;

Q is ~~independently~~: $-\text{NH}_2$, $-\text{NHR}^a$, $-\text{NR}^a_2$, or $-\text{NR}^a_3^+$; or:

Q is ~~independently~~ a polyhydric alcohol group, linked via an oxygen atom;

each R^a is ~~independently~~ linear or branched saturated C_{1-4} alkyl.

129. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^1 is ~~independently~~:

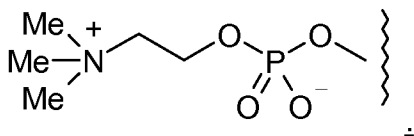


wherein:

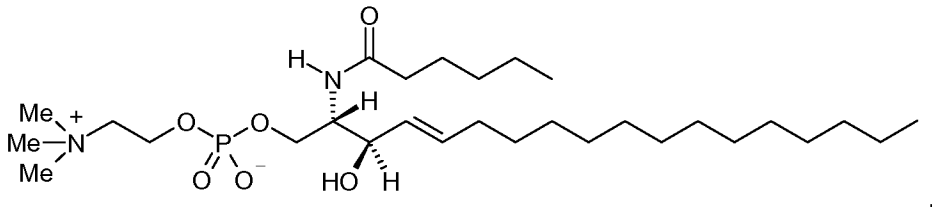
q is ~~independently~~ an integer from 0 to 5; and

each R^a is ~~independently~~ a C_{1-4} alkyl group.

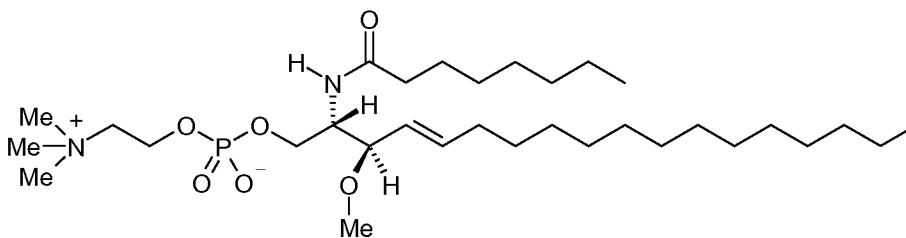
130. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein R^1 is ~~independently~~:



131. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula (" C_6 -SM"):



132. (Currently Amended) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula ("3-O-methyl-C₈-SM"):



133. (Currently Amended) A pharmaceutical formulation according to claim 128, wherein Q is ~~independently~~ a polyhydric alcohol group, linked via an oxygen atom.

134. (Currently Amended) A pharmaceutical formulation according to claim 133, wherein Q comprises ~~is formed from~~ a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

135. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said pharmaceutical formulation is suitable for parenteral administration.

136. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the pharmaceutical formulation is a liposomal pharmaceutical formulation.

137. (Previously Presented) A liposomal pharmaceutical formulation according to claim 136, wherein the liposomes of the liposomal pharmaceutical formulation are prepared using a mixture of lipids comprising, at least, vesicle-forming lipids and said short-chain sphingolipid.

138. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids and said short-chain sphingolipid.

139. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids, cholesterol, and said short-chain sphingolipid.

140. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phosphatidylcholines, cholesterol, and said short-chain sphingolipid.

141. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises fully hydrogenated soy phosphatidylcholine (HSPC), cholesterol, and said short-chain sphingolipid.

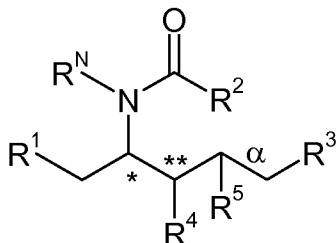
142. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises dipalmitoyl-phosphatidylcholine (DPPC), cholesterol, and said short-chain sphingolipid.

143. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a vesicle-forming lipid which is derivatized with a polymer chain.

144. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG).

145. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG2000-DSPE).

146. (Currently Amended) Caelyx® or Doxil® liposomes post-inserted with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group;

R² is independently C₃₋₉alkyl,

and is independently unsubstituted or substituted;

R³ is independently C₇₋₁₉alkyl,

and is independently unsubstituted or substituted;

R⁴ is independently -H, -OH, or -O-C₁₋₄alkyl;

R^N is independently -H or C₁₋₄alkyl;

the bond marked with an alpha (α) is independently a single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an S-configuration;

and pharmaceutically acceptable salts, ~~solvates, esters, and ethers~~ thereof.

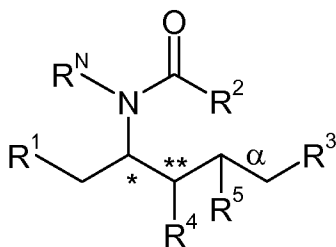
147. (Previously Presented) A method of making a pharmaceutical formulation according to claim 92, comprising the step of admixing said drug and said short-chain sphingolipid.

148. (Previously Presented) A method of treating a proliferative condition comprising administering to a patient in need of treatment an effective amount of a pharmaceutical formulation according to claim 92.

149. (Previously Presented) A method according to claim 148, wherein said proliferative condition is cancer.

150. (Previously Presented) A method according to claim 148, wherein the drug is doxorubicin or a salt thereof; and the proliferative condition is a proliferative condition that is treated by doxorubicin or a salt thereof.

151. (Currently Amended) A method of increasing the bioavailability and/or cellular uptake of a drug, which method includes the step of co-administering said drug with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group;

R² is independently C₃₋₉alkyl,

and is independently unsubstituted or substituted;

R³ is independently C₇₋₁₉alkyl,

and is independently unsubstituted or substituted;

R⁴ is independently -H, -OH, or -O-C₁₋₄alkyl;

R^N is independently -H or C₁₋₄alkyl;

the bond marked with an alpha (α) is independently a single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an S-configuration;

and pharmaceutically acceptable salts, ~~solvates, esters, and ethers~~ thereof.